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EXAMINER	
AEDER, SEAN E	

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/552,178	OKA ET AL.	
	Examiner	Art Unit	
	SEAN E. AEDER	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,7-9 and 11-19* is/are pending in the application.

4a) Of the above claim(s) *13-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5, 7-9, 11, 12, and 16-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The Amendments and Remarks filed 12/6/10 in response to the Office Action of 8/5/10 are acknowledged and have been entered.

Claims 18-19 have been added by Applicant.

Claims 1, 5, 7-9, and 11-19 are pending.

Claims 13-15 have been withdrawn.

Claims 1, 5, 11, 12, 16, and 17 have been amended by Applicant.

Claims 1, 5, 7-9, 11, 12, and 16-19 are currently under examination.

The following Office Action contains NEW GROUNDS of rejections necessitated by amendments, wherein the amendments change the scope of every pending claim.

Rejections Withdrawn

All previous rejections are withdrawn.

New Rejections Necessitated by Amendments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of: **a genus of genes and/or proteins selected in claim 1**. However, the written description in this case only sets forth the genes and/or proteins disclosed in Examples 8-11 as genes and/or proteins selected in claim 1. The specification does not disclose, and the art does not teach, the genus of genes and/or proteins selected in claim 1 as broadly encompassed in the claims.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common to that genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The inventions at issue in Lilly were DNA constructs per se, the holdings of that case is also applicable to claims such as those at issue here. Further, disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., F.3d, 2004 WL 260813,

at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of genes and/or proteins selected in claim 1 nor does it provide a description of structural features that are common to the genus. Since the disclosure fails to describe common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of the genes and/or proteins disclosed in Examples 8-11 is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, even though Applicant proposes methods of screening for possible members of the genus (see claim 1), the skilled artisan cannot envision the detailed chemical structure of the encompassed genus, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolation. The

compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only use of the genes and/or proteins selected in claim 1 wherein said genes and/or proteins selected in claim 1 are genes and/or proteins disclosed in Examples 8-11, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim 19 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of a **genus of self-organizing maps generated by Claim 17**. The specification does not disclose, and the art does not teach any the genus of self-organizing maps generated by Claim 17.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common to that genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The inventions at issue in Lilly were DNA constructs per se, the holdings of that case is also applicable to claims such as those at issue here. Further, disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., F.3d, 2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of self-organizing maps generated by Claim 17 nor does it provide a description of structural features that are common to the genus. Since the disclosure fails to describe common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure is insufficient to describe the genus.

Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, even though Applicant proposes methods of screening for possible members of the genus (see Claim 17), the skilled artisan cannot envision the detailed structure of the encompassed genus, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolation. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 5, 7-9, and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okabe et al (Cancer Research, March 2001, 61: 2129-2137) in view of Adorjan et al (US 2002/0192686 A1; 12/19/02) and in further view of Tang (World J Gastroenterol, 2001, 7(4): 445-454).

Okabe et al teaches a method of defining the differentiation grade of a tumor with genes selected by statistical analysis comprising determining the number of genes to define the differentiation grade of tumor and using microarrays based on expression level or pattern of genes of human liver tumor tissues, wherein the differentiation grade of tumor is non-cancerous liver, pre-cancerous liver, well differentiated HCC, moderately differentiated HCC, and poorly differentiated HCC and wherein the genes are differentially expressed between non-cancerous liver and pre-cancerous liver, precancerous liver and well differentiated HCC, well differentiated HCC and moderately differentiated HCC, or moderately differentiated HCC and poorly differentiated HCC (see pages 2136-2137, in particular). Okabe et al further teaches the importance of analyzing microarray data of tumor states using cluster analysis in order to see how

genes are expressed and gain insight into cellular processes involved in various classes of tumor (see page 2137, in particular).

Okabe et al does not specifically teach methods wherein the genes that have the highest Fisher ratios are selected by a supervised learning method in descending order of a Fisher ratio wherein the Fisher ratios are from a comparison between non-cancerous liver and pre-cancerous liver, pre-cancerous liver and well differentiated HCC, well differentiated HCC and moderately differentiated HCC, or moderately differentiated HCC and poorly differentiated HCC. However, these deficiencies are made up in the teachings of Adorjan et al. Further, Okabe et al does not specifically teach methods wherein genes and/or proteins are selected that have the highest Fisher ratios in comparison between (1) non-cancerous liver and pre-cancerous liver, (2) pre-cancerous liver and well differentiated HCC tumor, (3) well differentiated HCC tumor and moderately differentiated HCC tumor, and (4) moderately differentiated HCC tumor and poorly differentiated HCC tumor. However, these deficiencies are made up in the teachings of Tang et al.

Adorjan et al teaches a working example of selecting cancer markers that "reliably predict known tumor classes" by using a Fisher ratio, wherein highest Fisher ratios are selected by a supervised learning method in descending order of a Fisher ratio (see [0137]-[0145], in particular). Adorjan et al further teaches a Fisher ratio is a classical measure to assess the degree of separation between two classes and the Fisher ratio gives a high ranking for cancer markers where two classes are far apart compared to within class variations (see paragraphs 0104-0105, in particular).

Tang teaches subjects with HCV expression in normal liver leads to HCC (see Abstract and right column on page 445, in particular). Tang further teaches motivation to identify biomarkers for HCC progression (see Abstract, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to use any known calculation with the expression data of Okabe which would identify and characterize genes involved in carcinogenesis and tumor progression because Okabe motivates one to identify genes involved in carcinogenesis and tumor progression to further an understanding of the mechanisms of hepatocarcinogenesis, to reveal novel features of known genes, and identify biological factors involved in liver cancer (see right column of page 2129, in particular). Due to differences in results from each calculation which would identify genes involved in carcinogenesis and tumor progression, different calculations would result in different determinations of which genes are most important. Therefore, it would be obvious to perform the calculations of Adorjan et al on expression data that has previously been examined with a Mann-Whitney test to identify and characterize genes involved in carcinogenesis and tumor progression, and vice-versa. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for identifying and characterizing expression of genes involved in carcinogenesis and tumor progression by performing the calculations of Adorjan instead of the Mann-Witney test with the expression data of Okabe et al because Okabe et al teaches the importance of analyzing microarray data of tumor states using cluster analysis in order to see how genes are expressed and gain insight into cellular processes involved in various classes

of tumor (see page 2137, in particular) and Adorjan et al teaches a Fisher ratio is a "classical" measure to assess the degree of separation between two classes and the Fisher ratio gives a high ranking for cancer markers where two classes are far apart compared to within class variations (see paragraphs 0104-0105, in particular). Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Further, of ordinary skill in the art at the time the invention was made would have been motivated to select genes that have the highest Fisher ratios in comparison between (1) non-cancerous liver and normal liver expressing HCV (pre-cancerous liver), (2) pre-cancerous liver and well differentiated HCC tumor, (3) well differentiated HCC tumor and moderately differentiated HCC tumor, and (4) moderately differentiated HCC tumor and poorly differentiated HCC tumor when performing the combined method of Okabe et al in view of Adorjan et al because Okabe et al teaches such tissues, Okabe et al teaches the importance of identifying genes involved in carcinogenesis and tumor progression, Tang teaches motivation to identify biomarkers for HCC progression (see Abstract, in particular), and each of said comparisons would identify genes involved in carcinogenesis and each step of tumor progression. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for selecting genes that have the highest Fisher ratios in comparison between (1) non-cancerous liver and normal liver expressing HCV (pre-cancerous liver), (2) pre-cancerous liver and well differentiated HCC tumor, (3) well differentiated HCC tumor and moderately differentiated HCC tumor, and (4) moderately differentiated HCC tumor

and poorly differentiated HCC tumor when performing the combined method of Okabe et al in view of Adorjan et al because Okabe et al teaches such tissues, Okabe et al teaches the importance of identifying genes involved in carcinogenesis and tumor progression, and Tang teaches motivation to identify biomarkers for HCC progression (see Abstract, in particular). Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

In the Reply of 12/6/10, Applicant argues the cited references do not teach methods based on supervised learning and the Fisher ratio. Applicant further argues that the cited references do not teach identification of genes differentially expressed in each transition between five sequential stages of HCC. Applicant further argues that the Fisher ratio described in Adorjan is statistically inappropriate because the value of the formula can be either positive or negative.

The amendments to the claims and the arguments found in the Reply have been carefully considered, but are not deemed persuasive. In regards to the argument that the cited references do not teach methods based on supervised learning and the Fisher ratio, the calculations taught by Adorjan employ are based on supervised learning and the Fisher ratio (see [0137]-[0145], in particular).

In regards to the argument that the cited references do not teach identification of genes differentially expressed in each transition between five sequential stages of HCC, the cited references render obvious a method that would identify genes differentially expressed in each transition between five sequential stages of HCC as claimed.

In regards to the argument that the Fisher ratio described in Adorjan is statistically inappropriate because the value of the formula can be either positive or negative, the method comprising the Fisher ratio described in Adorjan is taught to "reliably predict known tumor classes" (see [0145] of Adorjan, in particular).

Claims 1, 5, 7-9, 11, 16, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okabe et al (Cancer Research, March 2001, 61: 2129-2137) in view of Adorjan et al (US 2002/0192686 A1; 12/19/02) and in further view of Tang (World J Gastroenterol, 2001, 7(4): 445-454) as applied to claims 1, 5, 7-9, and 11 above, and further in view of Bloch et al (US 6,728,642 B2; 4/27/04).

The combined teaching of Okabe et al, Adorjan et al, and Tang et al is discussed above.

The combined teaching of Okabe et al, Adorjan et al, and Tang et al does not specifically teach a method wherein a "minimum distance classifier" with data of selected genes is designed. However, these deficiencies are made up in the teachings of Boch et al.

Boch et al teaches a "minimum distance classifier" is a well-known cluster identification algorithm (see paragraph 0098, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to design minimum distance classifiers (instead of the leave-one-out calculation of Adorjan) with the genes identified by the method of Okabe et al, Adorjan et al, and Tang et al because Boch et al teaches a "minimum distance classifier" is a

"well-known" cluster identification algorithm (see paragraph 0098, in particular), and Okabe et al teaches the importance of analyzing microarray data of tumor states using cluster analysis in order to see how genes are expressed and gain insight into cellular processes involved in various classes of tumor (see page 2137, in particular). One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for designing minimum distance classifiers with the genes identified by the method of Okabe et al, Adorjan et al, and Tang et al because Boch et al teaches a "minimum distance classifier" is a "well-known" cluster identification algorithm (see paragraph 0098, in particular). Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Further, one of ordinary skill in the art at the time the invention was made would have been motivated to use results from the method taught by the combined references to define the differentiation grade of a tumor by determining expression levels or patterns of genes selected by the combined method in a liver tissue sample of unknown differentiation grade and applying the minimum distance classifier generated by the method taught by the combined references because such a method would inform a patient as to whether a tumor has progressed. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for using results from the method taught by the combined references to define the differentiation grade of a tumor by determining expression levels or patterns of genes selected by the combined method in a liver tissue sample of unknown differentiation grade and applying

the minimum distance classifier generated by the method taught by the combined references because such a method would inform a patient as to whether a tumor has progressed. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

In the Reply of 12/6/10, Applicant argues that one would not have been motivated to implement the minimum distance classifier of Bloch to arrive at the present invention because the present invention uses the minimum distance classifier for validating genes selected by the Fisher ratio based on supervised learning and Bloch uses the minimum distance classifier to identify clusters and to elucidate relationships.

The amendments to the claims and the arguments found in the Reply of 12/6/10 have been carefully considered, but are not deemed persuasive. In regards to the argument that one would not have been motivated to implement the minimum distance classifier of Bloch to arrive at the present invention because the present invention uses the minimum distance classifier for validating genes selected by the Fisher ratio based on supervised learning and Bloch uses the minimum distance classifier to identify clusters and to elucidate relationships, Applicant is arguing limitations not recited in the claims. The claims do not recite that the minimum distance classifier is to validate genes.

Claims 1, 5, 7-9, 11, 12, and 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okabe et al (Cancer Research, March 2001, 61: 2129-2137) in view

of Adorjan et al (US 2002/0192686 A1; 12/19/02) and in further view of Tang (World J Gastroenterol, 2001, 7(4): 445-454) and further in view of Bloch et al (US 6,728,642 B2; 4/27/04) as applied to claims 1, 5, 7-9, 11, 16, and 18 above, and further in view of Tamayo et al (PNAS, 1999, 96: 2907-2912).

The combined teachings of Okabe et al, Adorjan et al, Tang et al, and Bloch et al do not specifically teach generating a self-organizing map (SOM) with the selected genes and/or applying the SOM to expression levels or patterns of the selected genes detected in a liver tissue sample of unknown differentiation grade. However, these deficiencies are made up in the teachings of Tamayo et al.

Tamayo et al teaches advantages of a method of interpreting patterns of gene expression with SOM to characterize differentiation (see page 2907, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to generate a self-organizing map (SOM) with the selected genes in order to interpret and visualize the gene expression patterns of HCC differentiation because SOM is a neural network algorithm widely used for clustering and is well known as an efficient tool for the visualization of multidimensional data (see right column of page 2907 of Tamayo et al). One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for generating a self-organizing map (SOM) with the selected genes in order to interpret and visualize the gene expression patterns of HCC differentiation because Tamayo et al teaches a method of interpreting patterns of gene expression with SOM to characterize differentiation (see Abstract, in particular). Therefore, the invention as a whole would

have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Further, one of ordinary skill in the art at the time the invention was made would have been motivated to use results from the method taught by the combined references to define the differentiation grade of a tumor by determining expression levels or patterns of genes selected by the combined method in a liver tissue sample of unknown differentiation grade and applying SOM generated by the method taught by the combined references because such a method would inform a patient as to whether a tumor has progressed. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for using results from the method taught by the combined references to define the differentiation grade of a tumor by determining expression levels or patterns of genes selected by the combined method in a liver tissue sample of unknown differentiation grade and SOM generated by the method taught by the combined references because such a method would inform a patient as to whether a tumor has progressed. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Summary

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SEAN E. AEDER whose telephone number is (571)272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Misook Yu can be reached on 571-272-0839. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sean E Aeder/
Primary Examiner, Art Unit 1642